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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,196	01/24/2002	Y. Tom Tang	039386-0220	3875

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,196	TANG ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed February 21, 2006 is acknowledged and entered. Claims 3-11 are pending and under examination.

Claim Rejections - 35 USC § 112

2. (*New Rejection*) Claims 3-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims, as amended, recite, "an amino acid sequence having at least about 95% sequence identity to an amino acid sequence of SEQ ID NO: 2".

It is unclear what sequences are encompassed by "at least about 95% sequence identity". The metes and bounds of the claims cannot be determined because the specification fails to define what the term in question means. Lacking a descriptive definition, one of skill in the art would not know whether a polypeptide having 50% sequence identity with the assigned function (associated with cell proliferation) would qualify as "at least about 95% sequence identity".

It is also unclear whether "an amino acid sequence having at least about 95% sequence identity to an amino acid sequence of SEQ ID NO: 2" encompasses an amino acid sequence having at least about 95% sequence identity to a fragment of SEQ ID NO: 2. If this is not the meaning that Applicant intends, then suggested language to clarify the claims is, "95% sequence identity to the amino acid sequence of SEQ ID NO: 2". The claims would then be understood to encompass a sequence that has identity to the full-length sequence of SEQ ID NO: 2, not just a fragment of SEQ ID NO: 2.

Response to Arguments

3. The rejection of claims 3-11 under 35 U.S.C. 101 for not being supported by either a specific, substantial and credible asserted utility, or a well established utility, is maintained for reasons of record. Applicant's arguments filed February 21, 2006 have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily drawn to the following:

- Applicant argues that the claimed invention is supported by credible, asserted utilities relating to cell proliferation. Applicant points out that the application is drawn to "molecules associated with cell proliferation", thus, MACP-2 is associated with cell proliferation, as are all of the polynucleotides disclosed in the application. Applicant points to the acronym, MACP-2, which stands for molecules associated with cell proliferation. The claims, as amended, also recite this activity.
    - In response to Applicant's argument, the Office recognizes that Applicant has asserted a utility for the claimed polynucleotides. The Office also recognizes what MACP-2 stands for, and what the specification is directed to. Assigning a function to a polynucleotide and calling the polynucleotide by that function, does not mean that the polynucleotide has that function. Evidence is required to substantiate the assertion. While the threshold for utility is low, Applicant has not even met this low threshold such that the asserted utility is credible. The asserted utility for the invention is not credible, as outlined previously.
- Applicant argues that the utility requirement for the claims has been met because expression of MACP-2 is correlated with proliferative diseases, in particular prostate

cancer. Applicant points to Tables 1, 3 and 4 that demonstrate that MACP-2 is associated with prostate cancer, and that MACP-2 nucleotide is found in 71.4% of cDNA libraries that are proliferative in nature.

- In response to this argument, the Office has considered the data presented in Tables 1, 3 and 4 of the specification. However, these data do not demonstrate that MACP-2 is indicative of prostate cancer or any other proliferative disease. The data show that the MACP-2 nucleotide is present in certain libraries, but Applicant has not provided evidence that detection of MACP-2 in prostate cancer patients is any different from detection of MACP-2 in healthy individuals. According to one of skill in the art, the presence of MACP-2 in a library derived from a prostate cancer patient fails to directly translate to diagnosis without further testing.

- Applicant argues that one of skill in the art would recognize the link between MACP-2 and cell proliferative disease, particularly prostate cancer. In view of data, MACP-2 is useful for diagnosing disease.

  - In response to this argument, lacking a connection between MACP-2 and proliferative disease and prostate cancer, one of skill in the art would not recognize how MACP-2 is useful. The instant claims are drawn to polynucleotides that encode a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as MACP-2, or of nucleic acids encoding such or fragments thereof, the instant invention is incomplete. In

the absence of any functional or biological significance of this protein, there is no readily apparent use for it.

- Applicant also argues that Wissmann *et al.* (*J. Pathol.* 201(2):204-212, 2003, "Wissmann") is evidence that MACP-2 is a useful diagnostic marker for primary prostate cancers.
    - In response to this argument, the examiner has considered the Wissmann reference. Wissmann teaches that MACP-2 (WIF1) was down-regulated in 64% of primary prostate cancers (abstract). Wissmann also teaches that there is no correlation between WIF1 down-regulation and tumor stage or grade for prostate, breast or non-small cell lung carcinomas. Wissmann concludes that WIF1 expression may be an early event in tumorigenesis.
    - It is unclear how Applicant can argue that MACP-2 is present in 71.4% of cDNA libraries of proliferative nature, but absent in 64% of primary prostate cancers. Either MACP-2 is present or it is not present. These are conflicting data and conflicting arguments. Based on Applicant's presentation, if one were to use MACP-2 as a marker for prostate cancer, the absence of MACP-2 would be tested. However, given that Applicant is also assuming that MACP-2 is present in 71.4% of cDNA libraries of proliferative nature, one would also be testing for its presence. Clarification is requested.
- Applicant addresses this clarification request in the response filed February, 21, 2006. Applicant asserts that Wissmann reports on a differential gene expression analysis of particular genes in prostate cancer. Applicant asserts that Wissmann defines

differential expression as requiring that the gene must (1) be expressed in at least 50% of prostate tumor patients, (2) be up-regulated or down-regulated in at least 10% of tumor samples, and (3) the degree of up- or down-regulation should be at least two-fold (page 208, col. 1, second paragraph). Applicant asserts that Wissmann further shows that expression of the polynucleotide encoding MACP-2 is down-regulated at the RNA level in 64% of MACP-2-expressing tumors (page 208, col. 1, third and fifth paragraphs). Applicant argues that these data are consistent with the disclosure of the present application which indicates that MACP-2 is associated with cell proliferative disorders.

- In response to Applicant's arguments, the Office has considered the factors that Wissmann uses to determine differential gene expression of particular genes in prostate cancer. With regard to the first factor, the instantly claimed polynucleotide has not been demonstrated as expressed in at least 50% of prostate tumor patients. While the Tables 1, 3 and 4 of the instant specification disclose that MACP-2 is associated with prostate cancer, and that MACP-2 nucleotide is found in 71.4% of cDNA libraries that are proliferative in nature, this is not sufficient to support the conclusion that the instantly claimed gene(s) is expressed in at least 50% of prostate tumor patients. The cDNA libraries were not specific to prostate tumor samples.
- With regard to the second and third factors, Applicant has not demonstrated that the claimed genes are up-regulated or down-regulated in at least 10% of tumor samples, nor that the genes are up- or down-regulated at least two-fold. It is

unclear what population of tumor samples Wissmann is referring to. Regardless, Wissmann shows that the polynucleotide encoding MACP-2 is down-regulated at the RNA level in 64% of MACP-2-expressing tumors. This is not indicative of the second factor, namely, Wissmann only measured down-regulation in tumors that are already known to express MACP-2. The second factor requires that the gene be up- or down-regulated in 10% of tumors, not just the tumors that were pre-selected because of the expression of MACP-2. Wissmann's teachings about MACP-2 are also not indicative of the third factor because the population that Wissmann used to demonstrate 64% down-regulation was only in tumor samples expressing MACP-2, instead of tumor samples generally.

In summary, the claims polynucleotides with the claimed function are not supported by the specification. The differential gene analysis of Wissmann has not been adequately met by Applicant's work or that of Wissmann's with regard to SEQ ID NO: 2 and 7. Therefore, the claims remain rejected for lack of utility.

4. Claims 3-11 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility, or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. Claims 3-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Previously, claims 3, 5-7 and 9-11 were not included in this rejection, however, Applicant has amended the claims to encompass polynucleotides encoding sequences having at least about 95% sequence identity to an amino acid sequence of SEQ ID NO: 2, or SEQ ID NO: 7, respectively. The polynucleotide sequences encode polypeptides hat are associated with cell proliferation, a utility for which Applicant is not entitled (see rejections above).

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily drawn to the following:

- Applicant argues that the polypeptides that share 95% sequence identity to SEQ ID NO: 2 are adequately described in view of Table 2, page 51 of the specification. The Table shows potential glycosylation sites, signature sequences, and potential phosphorylation sites. The same argument is made for polynucleotides that are 95% sequence identical to SEQ ID NO: 7.
- Applicant points to the Synopsis of Written Description Guidelines from the USPTO. Applicant points to Example 14, where a single species was deemed representative of the genus because (1) all members have at least 95% structural identity with the reference sequence, and (2) because of the present of the assay which applicant provided for identifying all of the at least 95% identical variants which have the specified function.
    - In response to Applicant's arguments, the examiner is familiar with the Synopsis of Written Description Guidelines from the USPTO. In Example 14, two criteria were met. Applicant has not met either criteria. With regard to the first factor,

Applicant's claims recite, "at least about 95%", which is not the same in Example 14. With regard to the second factor, the assay for which Applicant provides for identifying all of the at least about 95% identical variants have a specific function that lack utility for the reasons discussed above. Therefore, Applicant's claims are not adequately provided for because the criteria have not been met, as outlined in Example 14.

- The Office has considered the information provided in Table 2 regarding SEQ ID NO: 2. Even though Applicant argues that 95% sequence identity allows only 19 amino acid changes, one of skill in the art would not know what variants of 90% are acceptable. Even if the claims were limited to conservative substitutions, one would not know which variants are acceptable because the disclosure fails to provide a detailed description directed to the intended variants of the polypeptide of SEQ ID NO: 2, or the polynucleotide of SEQ ID NO: 7, including critical features of such that should be conserved. It is not sufficient to name the claimed variant nucleic acids that can encode for polypeptides comprising 95% identity to SEQ ID NO: 2, or the variant polypeptides without disclosure of what features define the claimed genus. The disclosure fails to describe the common attributes or characteristics that identify the members of the genus.
- The Office agrees that description of a representative number of species is sufficient to meet the written description requirement, however, Applicant has not done this. Applicant has only provided one amino acid sequence, and one DNA

sequence. This disclosure is not supportive of claims to sequences that are any less than 100% identical to SEQ ID NO: 2 or SEQ ID NO: 7.

In summary, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is a polypeptide comprising SEQ ID NO: 2, and a polynucleotide comprising SEQ ID NO: 7. No active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.

Conclusion

6. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 4/12/2006

Stacy B. Chen
Primary Examiner
April 12, 2006